INtegrative approaches for Optimizing Recognition, Management and Education of concussion at the community sports level (INFORMED-1)

A randomised controlled trial of a telehealth program for providing more accessible and personalised care of individuals with concussion.

Chief Investigator:
Prof. Biswadev Mitra

School of Public Health & Preventive Medicine, Monash University

P: +61 3 9076 2782
F: +61 3 9076 2699
E: biswadev.mitra@monash.edu

The Alfred Hospital Ethics Committee ID: 128/23~~TBA~~

Monash University Human Research Ethics Committee (MUHREC) ID: TBA

ANZCTR Identifier: TBA

Contents

ABBREVIATIONS

AE	Adverse event
AFL	Australian Football League
CI	Confidence interval
CRF	Case report form
CRT5	Concussion Recognition Tool 5
ED	Emergency Department
GP	General Practitioner
HREC	Human Research Ethics Committee
INFORMED-1	INtegrative approaches for Optimizing Recognition, Management and Education of concussion at the community sports level - 1
mTBI	mild Traumatic Brain Injury
NHMRC	National Health and Medical Research Council
PICF	Patient Information and Consent Form
PICO	Population, Intervention, Comparator, Outcomes
PPCS	Persistent post-concussion symptoms
RCT	Randomised Controlled Trial
RR	Relative risk
RTP	Return to Play
RPQ	Rivermead Post-concussion Questionnaire
SAE	Serious adverse event
SOC	Standard of Care
SRC	Sports-related concussion
SUSAR	Suspected unexpected serious adverse reaction
TBI	Traumatic Brain Injury
VAFA	Victorian Amateur Football Association
VVED	Victorian Virtual Emergency Department

1. ABSTRACT

(References omitted from abstract and included in subsequent sections only)

Concussion, or mild traumatic brain injury (mTBI), is defined as the acute neurophysiological event related to blunt impact or other mechanical energy applied to the head or nearby regions. Sports-related concussion (SRC) occurs in the setting of sports and often results in short-lived impairment of neurological function causing symptoms such as confusion, headache, dizziness, fatigue, visual disturbance, balance problems, noise and/or light intolerance, mental slowness and fogginess and sleep disturbance that typically resolve spontaneously. However, these symptoms persist in 10-20 percent of cases and are termed Persistent Post Concussion Symptoms (PPCS).

Concussion is common and costly. In the Australian football context, an average of 7 head injuries per team per season has been estimated. Concussion carries long-term consequences for a significant number of those injured.

Diagnosing SRC is difficult for a number of reasons, including the fact that the initial observation of the head impact and subsequent signs associated with concussion is usually undertaken by non-clinicians in the community sports setting. Those monitoring for suspected concussion are often reliant upon the athlete's report of symptoms. Athletes may not report symptoms to avoid missing games. These factors can result in failure to seek a diagnosis or misdiagnosis, which places the athlete at risk of prolonged recovery – particularly in the case of repeated head impacts, which may worsen symptoms.

Managing SRC is also challenging, both in the immediate aftermath of the head injury and the long-term persistent post-concussion symptoms (PPCS). Best practice is poorly understood and inadequately implemented, particularly in the community setting. Unsafe and premature return to play (RTP) can have a cumulative burden on athletes and our community.

Telehealth has been used since the 1990s and shown to be effective for many critical and non-critical care conditions. These services improve access to clinical expertise, contribute to greater equity, shorten travel/waiting times and times to decisions, especially in rural and regional settings. The COVID-19 pandemic has further increased use of telehealth. Concussion is one condition that would benefit from remote expertise given its challenges in diagnosis and management. Use of telehealth to diagnose and treat concussion is yet to be explored in a rigorous clinical trial.

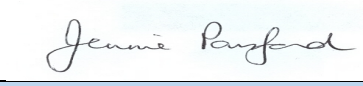
We aim to investigate the role of telehealth in diagnosis and management of SRC. We hypothesise that the incidence of SRC across Australia, particularly in the community settings, together with the complex nature of its diagnosis and management, make telehealth a suitable (i.e., safe and effective) means of providing more accessible and personalised concussion care.

This project- INFORMED-1 will be an open-label randomised controlled trial (RCT). The *Intervention (I)* will be a multidisciplinary telehealth service for assessment of community football players after head injury. The *Comparator (C)* will be current standard of care, which in the Australian context includes online resources, mobile phone applications, medical reviews as sought out by the players and/or trainers depending on the symptoms – typically involving GP review in the first instance, based on standard club policy. The primary *Outcome* will be the proportion of players diagnosed with concussion at 7-days post head injury. Secondary outcomes will include improvement in concussion symptoms, adherence to current RTP guidelines, access to clinical specialists, and satisfaction with the program.

Our research question is, amongst Australian football players in the VAFA league suffering a sustained head impact and suspected concussion(P), does a multidisciplinary telehealth program (I), increase the proportion of players diagnosed with concussion (O1), and improve their symptoms, adherence to RTP guidelines, access to clinical specialists, and satisfaction with the program (O2) compared to the provision of current standard of care (C)?

2. MANAGEMENT COMMITTEE AUTHORISATION PAGE

We, the management committee, have read the attached protocol and authorise it as the official protocol for the study entitled: **INFORMED-1**

CHIEF INVESTIGATOR		DATE	
Prof. Biswadev Mitra			
LEAD INVESTIGATOR		DATE	
Dr. Alexander Olaussen			
INVESTIGATOR		DATE	
Dr Stuart McDonald			
INVESTIGATOR		DATE	
Prof. Jennie Ponsford		12/02/2023	
INVESTIGATOR		DATE	
Associate Prof. Sandy Shultz			
INVESTIGATOR		DATE	
Associate Prof. Catherine Willmott		06/02/2023	
INVESTIGATOR		DATE	
Prof. Terence J. O'Brien			
INVESTIGATOR		DATE	
Prof. Michael O'Sullivan			
INVESTIGATOR		DATE	
Dr. Michael Makdissi			
INVESTIGATOR		DATE	
Dr Zhibin (Ben) Chen			

INVESTIGATOR		DATE	
Dr Jonathan Reyes			

3. STUDY ADMINISTRATION STRUCTURE

3.1 Coordinating Centre and Data Management Centre

3.1.1 Responsibilities

Responsible for all aspects of study management including:

- Management of study budget and liaison with funding bodies
- Final protocol
- Case Report Form design
- Database development, maintenance and administration
- Data management
- Protocol training of principal investigators and research coordinators
- Protocol training of critical care nurse, emergency physician, neurologists and neuropsychologists
- Management of regulatory affairs
- Management of study set up including assistance with HREC applications
- Organisation of investigator meetings
- Adherence to local HREC guidelines and reporting requirements
- Adverse event reporting to HREC and the Coordinating centre, in accordance with the study protocol

3.1.2 Meetings

Fortnightly

3.3 Study Contact Details

3.3.1 Chief Investigator

Professor Biswadev Mitra
Level 3 / 553 St Kilda Road
Melbourne VIC 3004 Australia
P: +61 3 9076 2782
E: biswadev.mitra@monash.edu

3.3.2 Coordinating Centre

Alfred Health Emergency Service
55 Commercial Rd
Melbourne VIC 3004, Australia

4. BACKGROUND & RATIONALE

4.1 Background summary

Concussion, or mild traumatic brain injury (mTBI), is defined as "the acute neurophysiological event related to blunt impact or other mechanical energy applied to the head, neck or body (with transmitting forces to the brain), such as from sudden acceleration, deceleration or rotational forces."[1] Such forces may be sustained in a number of situations, including motor vehicle crashes, assault, falls, or during sports. Sports-related concussion (SRC) is defined "a traumatic brain injury induced by biomechanical forces that typically results in the rapid onset of short-lived impairment of neurological function that resolves spontaneously".[2]

Concussion is common, with an estimated annual incidence of up to 1.2% in community settings.[3] In the Australian football context, the incidence equates to an average of 7 injuries per team per season.[4] Concussion typically causes symptoms including temporary loss of consciousness and/or confusion, headache, dizziness, fatigue, visual disturbance, balance problems, noise and/or light intolerance, mental slowness and fogginess and sleep disturbance that typically resolve spontaneously. Whilst it is thought that the majority of athletes recover within the first two weeks post-injury, longitudinal prospective observational studies have shown that as many of 55% have ongoing symptoms 14 days after head injury.[5] A significant number of these individuals have persistent symptoms and are termed as having Persistent Post Concussion Symptoms (PPCS).[6–8] The financial costs of concussion are significant.[9,10] Although current guidelines recommend return to play (RTP) after 12 days, this may not adequately reflect the time to recovery observed in the literature. One study of women's rugby estimated a pooled concussive injury burden of more than a month (i.e. 33.2 days),[11] and a 2-year prospective trial showed that 55% of patients had ongoing symptoms ant 14 days and 23% of participants still had ongoing symptoms after 4 weeks[5]. Sex differences in PPCS have also been reported, with a growing amount of evidence suggesting that female athletes are at greater risk of prolonged PPCS.[11]

Diagnosing SRC is difficult, as it relies on self-report and subjective brain function measures, requires honesty and cooperation from the injured player , as well as in-depth operator training to deliver prescriptive tests. The fact that initial screening is sometimes done by non-clinicians in the community sports setting further jeopardises the diagnosis rate and accuracy, placing the athlete at risk of prolonged recovery – particularly in the case of of continuing to play with a suspected concussion with repeated head impacts.[12,13] The Concussion Recognition Tool 5 (CRT5) is one widely used and validated tool for screening of SRC and was designed to assist non-medically trained individuals to recognise the signs and symptoms of possible SRC[14]. The CRT5 also guides the removal of a player and suggestion on whether medical attention should be sought. We will use this tool on our website and as safety screening to ensure that patient does not suffer more serious head injury. Diagnosis by a qualified medical practitioner is recommended in all cases of suspected concussion in the sporting context. The main reasons for why individuals do not seek medical evaluation after suspected concussion are beliefs about it not being serious enough, desire to continue playing and a lack of access to medical professionals.[15] Further highlighting the potential benefits of telehealth.

Whilst there is a growing interest in objective biomarkers as a means of augmenting the diagnosis of concussion, such as saliva testing[16], blood tests[17], and virtual reality[18], improving the use of currently available and validated clinical and cognitive screening strategies should be explored.

Managing SRC, both in the immediate aftermath of the head injury and the long-term PPCS, is also challenging. Best practice management of SRC is poorly understood and inadequately implemented, particularly in the community setting. Both parents and athletes are frequently unaware of the symptoms of concussion.[19] This may result in delay or

misdiagnosis with an unsafe and premature return to play RTP. Parents with general medical training have been shown to recognise symptoms more accurately than parents without first aid certification (p = .01)[19], thus suggesting there is an advantage to expert clinical assessment.

Telehealth has been shown to be effective for many critical care conditions such as stroke,[20] and myocardial infarction,[21] as well as for non-critical emergencies,[22] since the 1990s. These services improve access to clinical expertise, contribute to greater equity, shorten travel/waiting times and time to decisions.[23,24] The use and impact of telehealth have been particularly beneficial for patients in rural and regional settings.[25,26] Given the challenges with diagnosing SRC, including the clinical complexity and lack of access to specialists, telehealth may be a suitable alternative to deliver more specialised care, earlier, to most individuals with suspected concussion.

We hypothesise that telehealth a will be i.e. safe and efficient for providing more accessible and personalised concussion care.

4.2 Research question

The research question for this trial is formulated in the answerable PICO (population, intervention, comparator, outcomes) format[27].

Our research question is, amongst Australian football players in the VAFA league suffering a head injury (P), does a multidisciplinary – consisting of neuropsychologists, physiotherapists, emergency physicians, neurologists, critical care nurse, neuroscientists and sports physicians - telehealth program (I), increase the proportion of players diagnosed with concussion (O1), and improve their symptoms, adherence to RTP guidelines, access to clinical specialists, and satisfaction with the program (O2) compared to the provision of current standard of care (C)?

Population	All adult (≥18 years old) players in the Victorian Amateur Football Association (VAFA) who have sustained a head impact and suspected concussion
Intervention	Multidisciplinary telehealth consultation, consisting of neuropsychologists, physiotherapists, emergency physicians, neurologists, critical care nurse, neuroscientists and sports physicians
Comparator	Standard of care including information on currently available online resources, including AFL return to play advice
Outcome -primary	Proportion of players who have been given a diagnosis of concussion at 7 days post head injury
Outcome-secondary	a) Longitudinal data on concussion symptoms on the Rivermead Post-concussion Questionnaire (RPQ) at 3 time-points b) The proportion of adherence to current RTP guidelines. c) Access to clinical specialists d) Satisfaction with the program

4.3 Co-enrolment and competing studies

The management committee will consider all requests for co-enrolment with this trial. The criteria for assessing whether co-enrolment would be allowed will follow the guidelines published as the SPICE-8 criteria.[28]

Table 1. The SPICE-8 criteria that must be considered in assessing whether co-enrolment in a proposed trial (Trial B) should be allowed for patients already enrolled in a trial that is underway (Trial A)

Criterion	Description
Biological interaction between interventions	There should be little or no plausible biological interaction between the experimental interventions in the two trials; *or* If there is a potential biological interaction, the interventions in Trial B would have been received by the patients in Trial A in approximately the same proportions, had they received only routine clinical care rather than that provided because they were enrolled in Trial B.
Effects on protocol compliance and intercurrent care	There should be little likely influence on Trial A protocol compliance or intercurrent care resulting from enrolment in Trial B.
Equal allocation to trial groups	The treatment groups in Trial A should have equal chances of being allocated to the treatment groups in Trial B.
Treatment restrictions	Any protocol-mandated treatment restrictions in the intervention or control group of Trial B should not alter the treatment of either group in Trial A.
Mandated intercurrent treatments	Intercurrent treatment requirements in the control or intervention groups of Trial B should not substantially alter the treatments of patients in Trial A.
Outcome ascertainment	Ascertainment of outcomes in Trial B should not affect the outcomes in Trial A.
Clinical decision making	Information collected in Trial B that would not otherwise have been collected, and that is contemporaneously available, should not alter clinician decision making in any way that might affect the interventions, intercurrent care or outcomes of Trial A.
Adverse event procedures	The procedure for dealing with an adverse event in Trial B should not have an impact on the conduct of Trial A.

Figure 1: SPICE-8 criteria

4.4 Concomitant Care

Standard clinical care and advice for players with a head injury will be applied. All other investigations and treatment of the patient will be conducted as per usual.

4.5 Design

The design of this study is a prospective, single-centre, open-label randomised controlled trial.

4.5.1 Inclusion criteria

1. Adult patients (age ≥18 years);
2. Medicare eligibility
3. Head injury sustained during sports event (either matches or training) through VAFA;
4. Concussion suspected by either club trainer, medical professionals, or players themselves
5. GCS 13-15

4.5.2 Exclusion criteria

1. Adolescent (<18 years)
2. Moderate or severe Traumatic Brain Injury (TBI)
3. Intracranial haemorrhage
4. GCS<13

4.6 Methods

4.6.1 Randomisation

We will randomise using block randomisation (randomly selected block sizes of 4,6 or 8). The nurse will do the randomisation. We will use computerised randomisation method. Participants with suspected concussion will be referred either by themselves, club personnel or clinicians (e.g., their GP). Randomisation will occur after a critical care nurse has collected baseline data and ensured trial eligibility. The participant will have to provide consent prior to this contact (see sections 6.4 and 6.5). Prior to commencing the interview, the nurse will confirm that the participant has understood and agrees to the study.

4.6.2 Intervention

A multidisciplinary telehealth program with neuropsychologists, physiotherapists, emergency physicians, neurologists, critical care nurse, neuroscientists and sports physicians will be available to the participant. Among participants randomised to the telehealth arm, the consultation will be conducted primarily by a neuropsychologist or physiotherapist, rostered 4 half-days per week. The neuropsychologist will be co-located with a medical specialist (emergency physician or neurologist) for assessment of symptoms related to the head injury outside the scope of possible concussion (e.g. more than mild TBI) or an entirely alternative diagnosis. Follow-up consultations using telehealth will be scheduled at 7 days and 14 days and may also occur at greater frequency if recommended by the assessing team. Should the telehealth team feel the need for in-person assessment and management, including physiotherapy or occupational therapy for example, this will be facilitated. Additional nurse follow-up will occur at 30 days to assess satisfaction with the telehealth program. All other standard care processes will be continued as per normal clinical practice. The intervention arm will – in addition to their telehealth – be directed to out dedicated website to get the same information as the SOC arm.

4.6.3 Comparator

Participants randomised to the standard care arm will be provided with currently available online resources and mobile phone application (i.e. HeadCheck) for the assessment and management of concussion, including AFL's RTP advice.

Follow-ups will be conducted, on an observatory basis (i.e. not clinical assessments), by research nurses by telephone ~~at~~ on days 7~~,~~ and 14~~ and 30 days~~.

4.6.4 Outcomes

The primary outcome for this study is the diagnosis rate, whilst secondary outcomes include symptom improvements, RTP adherence, access to clinical specialists, and user satisfaction with the telehealth program.

Primary outcome

- The proportion of players diagnosed with SRC at 7 days. This will be collected by a binary question to the player: "Have you been diagnosed with concussion by a clinician (doctor, neuropsychologist, physiotherapist or occupational therapist)?"

Secondary outcomes

- Longitudinal data on concussion symptoms on the Rivermead Post-concussion Questionnaire (RPQ) at the 3 time-points
- The proportion of adherence to current RTP guidelines.
- Access to clinical specialists
- Satisfaction with the program

4.6.5 Potential confounders

Data will be collected on age, sex, past history including previous concussions, mechanism of injury, history of mental health issues, other injuries sustained, initial match day symptoms and all pre-enrolment diagnostics and management steps. (see s7.2)

5. STUDY PROCEDURES

5.1 Study participant capture

Any players in the VAFA league with a mild head injury sustained during match or training, within the previous 7 days, can be referred, either by themselves or club personnel. This will be done through a dedicated website, which is to be created for the INFORMED project. This website will follow the layout and logical flow of the Victorian Virtual Emergency Department (VVED)[29] as this is familiar both to clinicians and some patients, as well as having been approved by the Department of Health, Victoria.

5.2 Exclusion of moderate or severe brain injury

The exclusion of moderate to severe brain injury will be ensured by:

1. The initial self-directed screening through the use of our custom-built evidence-based online checklist which is designed to identify red flags that may indicate the need for emergency assessment, and
2. Nursing triage within 1 business day to assess participant safety, establish trial eligibility and randomisation.

5.3 Phone / online triage by critical care nurse

The critical care nurse will contact patients by phone, within 1 business day.

- collect baseline data of players
- screen for eligibility
- assign study ID
- Create a study enrolment log, which will link the study number to the patient's name.

5.4 Randomisation

We will randomise using block randomisation (randomly selected block sizes of 4,6 or 8). Randomisation will occur after a critical care nurse has collected baseline data and ensured trial eligibility. The nurse will do the randomisation using computer aided randomisation methods. This is an open-label trial and the research team and players will be aware of their allocation.

5.5 The two study arms

5.5.1 The standard of care (SOC) arm

The standard of care (SOC) arm will be directed to our dedicated website, which will house links to currently available resources, including

  - https://www.betterhealth.vic.gov.au/health/conditionsandtreatments/head-injuries-and-concussion
  - https://www.healthdirect.gov.au/concussion
  - https://aci.health.nsw.gov.au/__data/assets/pdf_file/0007/195154/NH700194-Mild-brain-injury-discharge-advice-for-adults.pdf
  - https://resources.afl.com.au/afl/document/2022/07/07/13577d34-be4b-4bcf-b131-b709da516eb8/Concussion-Management-in-Australian-Football-Poster.pdf?_ga=2.51831657.1700142125.1673848166-652702011.1673848166
  - Concussion in Sport Australia | Australian Sports Commission – https://www.concussioninsport.gov.au/
- Mobile phone applications
  - HeadCheck Concussion Management App
- AFL RTP advice
  - https://resources.afl.com.au/afl/document/2021/05/02/2b197edf-0f6f-4004-a3ee-0e0de4425de9/Return-to-Play-Following-Concussion-Checklist-

Form.pdf?_ga=2.81193815.1700142125.1673848166-652702011.1673848166

- "The earliest that a player may return to play (once they have successfully completed a graded loading program and they have obtained medical clearance) is on the 12th day after the day on which the concussion was suffered." (https://www.afl.com.au/clubhelp/policies/health-and-safety/concussion-management#:~:text=Any%20player%20who%20has%20suffered%20a%20concussion%20or%20is%20suspected,who%20is%20unconscious%20or%20injured.)

5.5.2 The intervention arm

Patients in the intervention arm will, in addition to receiving the same directions with regards to the website with information as the SOC arm, be scheduled (by the nurse) to an appointment with a neuropsychologist (or physiotherapist) via telehealth within the next few days. This video consult will take place on a Wednesday +/- Thursday and will have 8 slots of 45 – 60 minutes available. The consult will not be video recorded.

If during the assessment, the neuropsychologist or physiotherapist are concerned for the patient, they can seek advice from rostered on medical specialists (emergency physicians or neurologists) who will be virtually co-located for urgent assessment of symptoms related to the head injury outside the scope of a possible concussion.

The neuropsychologist / physiotherapist will perform an assessment of symptoms and tests of cognitive function. The primary outcome of this trial is the proportion of players that have been given a diagnosis of concussion. In both arms, the participants can be diagnosed by any medical practitioner. In the intervention arm the qualified specialist neuropsychologist or physiotherapist doing the assessment can also diagnose. This data will be collected as a binary question that will be asked by the research nurse conducting follow-ups on day 7.

5.6 Day 7 and day 14 Follow up

On day 7 and day 14, the patients, in both arms will be followed up by a research nurse. For patients in the telehealth group, this follow-up will occur immediately after the clinical consult. For patients in the SOC group, follow-up will occur by telephone. Data on key outcome variables will be collected. If ~~the~~ any patient from either arm has persistent symptoms on day 14, they will be offered to enrol in the iRecover trial an an interdisciplinary intervention that incorporates expertise from neuropsychology, physiotherapy, and medicine to target the primary factors thought to contribute to PPCSs (for more information, see ANZCTR Registry)[30]. Available from https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=384026&isReview=true

5.7 Day 30 follow up

On day 30 post head injury, a research nurse will collect further follow-up data from the intervention arm participants by telephone interview (See s7.2)

6. ETHICS

6.1 Guiding Principles

This study is to be performed in accordance with the ethical principles of the Declaration of Helsinki (June 1964 and amended 1975, 1983, 1989, 1996, 2000, 2008 and Note of Clarification 2002 and 2004), ICH GCP Notes for Guidance on Good Clinical Practice (CPMP/ICH/135/95) annotated with Therapeutic Goods Administration comments, NHMRC National Statement on Ethical Conduct in Research Involving Humans (March 2007)[31]; the New Zealand Interim Good Clinical Research Practice Guidelines (Volume 2 1998 and Volume 3 2000) and ICH GCP Notes for Guidance on Good Clinical Practice (CPMP/ICH/135/95).

6.2 Ethical issues of the study

We foresee no significant ethical issues with this study. All participants will be asked to provide informed consent. Participants will be free to withdraw from the trial at any time, ~~with the option to have~~and all existing data will be deleted.

6.3 Confidentiality of participant data

Patients will be randomised by the critical care nurse who is doing the phone triage. The patient will receive a study number. The Research Coordinator will compile a study enrolment log, which will link the study number to the patients' name. Subsequent data will be identified by the study number. The enrolment log and study data will be kept separately. Follow-up details of the patient will be collected including name, address and contact telephone numbers for the purpose of contacting the patient for subsequent reviews. The contact details will be forwarded to the coordinating centre. Study data will be entered into The Alfred Hospital Red-Cap database specifically designed for the study with restricted access via authenticated login using an email address and password combination. The contact details will be kept electronically in a secured database in RedCap. There will be no hard copies stored physically. As per the AlfredHealth Archiving/Storage of Research Records Guidelines, ~~The~~ the data will be retained ~~for 15 years~~ indefinitely. If, at some stage in the future, the Ethics Committee deems that storage is no longer required, the researchers will be notified and all materials will be destroyed in a secure manner. This would not occur until at least 15 years after completion of the study.

6.4 Informed consent

Patient Information and Consent Form (PICF) will be provided electronically to all participants. This information sheet provides a brief outline of the research, its requirements and the contact details of the local research coordinator who can explain the study to the participant and their relatives. The Red-Cap e-Consent platform will be used for the purpose of obtaining the consent of the participants. All participants will be emailed a copy of the PICF when they sign up.

The consent process will occur online via REDCap. The participants will be presented with the PICF in PDF form. They can print a hard copy and/or read this in their own time. The PICF will be presented on the website and can be read separate to the sign up and consenting phase. After signing up, the PICF will be sent electronically to the participants. There will be no signed hard copies of the PICF. If a participant requests a signed hard copy of the PICF, they will not be able to participate in the study. When the research nurse calls the participant within 1 business day of signing up, the participant will be explicitly asked whether they had any questions from the PICF or whether they would like any items clarified. The participant can withdraw at any time.

Readability will be ensured through the use of PDFs. The participants will sign the consent via the in-built signature field in REDCap.

All interaction between research staff and participants will take into consideration the potential stress and emotional factors associated with their head injury and ensure that their freedom to participate, actual or perceived, is not compromised.

6.5 Recruitment and consenting

The website www.informedtbi.org will be made aware to club trainers and players through a number of channels within VAFA. On this website, potential participants will screen themselves for eligibility. If they meet all the inclusion criteria and none of the exclusion criteria, they will be able to register for the trial.

The participants will populate a RedCAP contact form. REDCap is a secure web application for building and managing online surveys and databases. REDCap can be used to collect virtually any type of data in any environment and is compliant with Code of Federal Regulation 21 / Part 11, Federal Information Security Modernization (FISMA), Health Insurance Portability and Accountability Act (HIPAA), and General Data Protection Regulation (GDPR). It is specifically geared to support online and offline data capture for research studies and operations. The REDCap Consortium, a vast support network of collaborators, is composed of thousands of active institutional partners in over one hundred countries who utilize and support their own individual REDCap systems.

During the online registration, the participants will be presented withthe PICF, using the in-built e-Consenting features in Red-Cap.

The initial contact from us to the participants will be made by a research critical care study nurse, over phone or email, within 1 business day of registration. The nurse will confirm study eligibility and understanding of the PICF. At this time, eligible participants will be requested to electronically sign the consent form. A fully executed copy of the PICF will be sent to participants electronically (there will be no hard copies of the PICF).

7. DATA MANAGEMENT

7.1 Data collection methods

Data collection will be via a web-based data entry using the Red-Cap system. Data queries will be automatically generated via the electronic data collection database. Randomised patients will be followed up from a clinical trial point of view till day 14 post head injury. On day 30 a follow-up to assess satisfaction with the telehealth program will occur by the study nurse. (see s7.2)

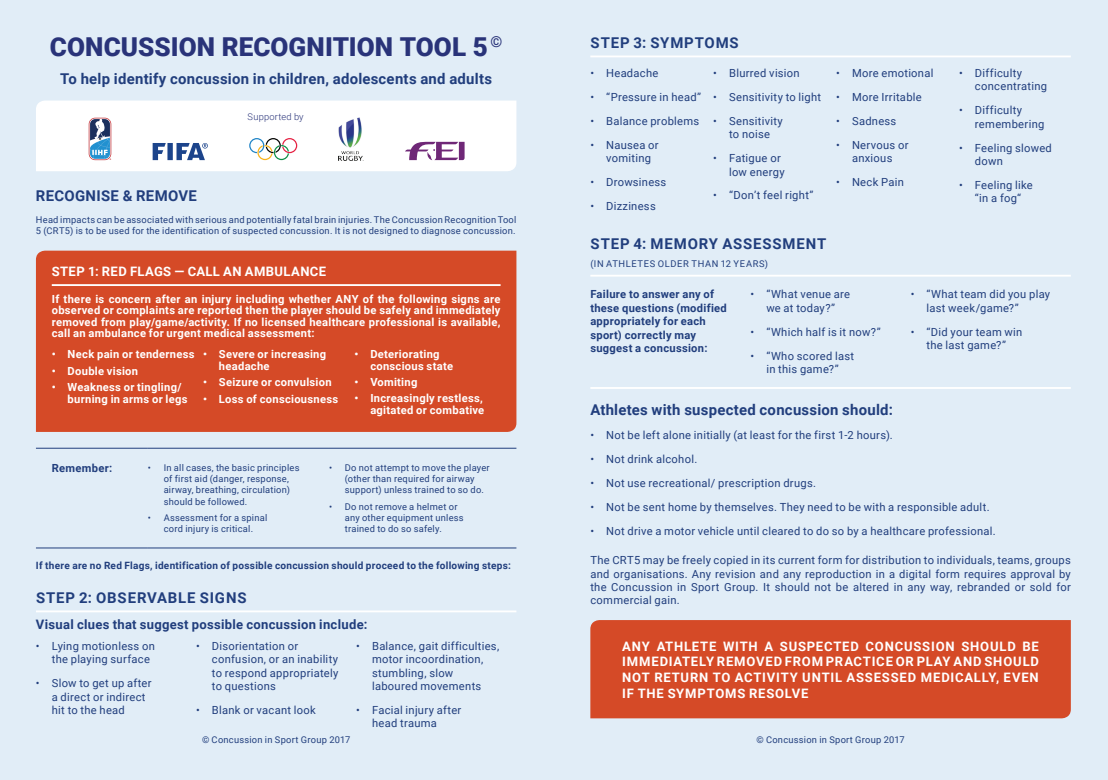
Alfred Health's REDCap will be used.
The contact details will be kept electronically in a secured database in REDCap.
There will be no hard copies stored physically.
Electronic data retention period will be ~~15 years~~indefinitely.
The website will be housed on multiple servers through the wix.com platform.
~~The data retention period for the website is 15 years.~~
The website will be hosted by Wix. Wix deploys and maintains technical and organisational security measures to protect the company's and our customers' data and assets. Details can be found here https://support.wix.com/en/article/wix-security-measures-overview.
No participant data will be collected or stored through the wix platform. The REDCap participant registration form will be displayed on the website, but data will be collected separately.
Access to the electronic data will be by the study coordinator Dr Alexander Olaussen and Chief Investigator Prof Biswadev Mitra. All participant data will be collected and stored in REDCap. If a participant withdraws from the study, this data will be deleted.
The identifiable data will be collected in REDCap. The study research nurse will contact the participant within 1 business day and when so doing create a study enrolment log, which will separate the research data from the contact details with a study ID. This process will create a study ID.

7.2 Data variables collected and data dictionary

Domain	Variable	Data dictionary	When is the data collected?			
Demographics			Enrolment	Day 7	Day 14	Day 30
	Caller's role	trainer, GP, club doctor, coach, other	✅	❌	❌	❌
	Caller's contact details	phone and email	✅	❌	❌	❌
	Age	Years	✅	❌	❌	❌
	Sex	M/F/Other	✅	❌	❌	❌
	Past Med Hx	free text	✅	❌	❌	❌
	Previous concussions (diagnosed and suspected)	binary (y/n)	✅	❌	❌	❌
	patient ID number	assigned on enrolment day	✅	✅	✅	✅
Incidence						
	date of injury	dd/mm/yyyy	✅	❌	❌	❌
	time of injury	HH:MM (24hrs)	✅	❌	❌	❌
	descriptions of events	free text	✅	❌	❌	❌
	first aid applied	free text	✅	❌	❌	❌
	removal from play	binary (y/n)	✅	❌	❌	❌
	match day CRT5	survey	✅	❌	❌	❌
Pre-consult assessment and treatment						
	ED	binary (y/n)	✅	❌	❌	❌
	GP	binary (y/n)	✅	❌	❌	❌
	Neuroimaging	binary (y/n)	✅	❌	❌	❌
	outcome of pre-consult Ax and Mx	free text	✅	❌	❌	❌
Concussion symptoms						
	Concussion symptoms (CRT5)	survey	✅	✅	✅	❌
	RPQ	survey	✅	✅	✅	❌
Telehealth arm (only)						
	length of tele-consultation	mins	✅	✅	✅	❌
	technical issues	free text	✅	✅	✅	❌
	Neuropsychology assessment	free text		✅	✅	❌
	neuropsychology recommendations	free text		✅	✅	❌
Outcomes						
	diagnosed with concussion	binary (y/n)	✅	✅	✅	❌
	RTP adherence	binary (y/n)	✅	✅	✅	❌
	access to clinical specialists	binary (y/n)	✅	✅	✅	❌
	Telehealth Usability Questionnaire	survey	❌	❌	❌	✅
	Client Satisfaction Questionnaire-8	survey	❌	❌	❌	✅
Adverse events						
	AEs	binary (y/n)	✅	✅	✅	❌
	SAEs	binary (y/n)	✅	✅	✅	❌
	SUSARs	binary (y/n)	✅	✅	✅	❌

7.2.1 CRT5

The Concussion Recognition Tool 5 (CRT5) is a widely used and validated tool for screening of SRC and was designed to assist non-medically trained individuals to recognise the signs and symptoms of possible SRC[14]. The CRT5 also guides the removal of a player and suggestion on whether medical attention should be sought.



CONCUSSION RECOGNITION TOOL 5©

To help identify concussion in children, adolescents and adults

Supported by

RECOGNISE & REMOVE

Head impacts can be associated with serious and potentially fatal brain injuries. The Concussion Recognition Tool 5 (CRT5) is to be used for the identification of suspected concussion. It is not designed to diagnose concussion.

STEP 1: RED FLAGS — CALL AN AMBULANCE

If there is concern after an injury including whether ANY of the following signs are observed or complaints are reported then the player should be safely and immediately removed from play/game/activity. If no licensed healthcare professional is available, call an ambulance for urgent medical assessment:

- Neck pain or tenderness
- Double vision
- Weakness or tingling/ burning in arms or legs
- Severe or increasing headache
- Seizure or convulsion
- Loss of consciousness
- Deteriorating conscious state
- Vomiting
- Increasingly restless, agitated or combative

Remember:

- In all cases, the basic principles of first aid (danger, response, airway, breathing, circulation) should be followed.
- Assessment for a spinal cord injury is critical.
- Do not attempt to move the player (other than required for airway support) unless trained to so do.
- Do not remove a helmet or any other equipment unless trained to do so safely.

If there are no Red Flags, identification of possible concussion should proceed to the following steps:

STEP 2: OBSERVABLE SIGNS

Visual clues that suggest possible concussion include:

- Lying motionless on the playing surface
- Slow to get up after a direct or indirect hit to the head
- Disorientation or confusion, or an inability to respond appropriately to questions
- Blank or vacant look
- Balance, gait difficulties, motor incoordination, stumbling, slow laboured movements
- Facial injury after head trauma

© Concussion in Sport Group 2017

STEP 3: SYMPTOMS

- Headache
- "Pressure in head"
- Balance problems
- Nausea or vomiting
- Drowsiness
- Dizziness
- Blurred vision
- Sensitivity to light
- Sensitivity to noise
- Fatigue or low energy
- "Don't feel right"
- More emotional
- More Irritable
- Sadness
- Nervous or anxious
- Neck Pain
- Difficulty concentrating
- Difficulty remembering
- Feeling slowed down
- Feeling like "in a fog"

STEP 4: MEMORY ASSESSMENT

(IN ATHLETES OLDER THAN 12 YEARS)

Failure to answer any of these questions (modified appropriately for each sport) correctly may suggest a concussion:

- "What venue are we at today?"
- "Which half is it now?"
- "Who scored last in this game?"
- "What team did you play last week/game?"
- "Did your team win the last game?"

Athletes with suspected concussion should:

- Not be left alone initially (at least for the first 1-2 hours).
- Not drink alcohol.
- Not use recreational/ prescription drugs.
- Not be sent home by themselves. They need to be with a responsible adult.
- Not drive a motor vehicle until cleared to do so by a healthcare professional.

The CRT5 may be freely copied in its current form for distribution to individuals, teams, groups and organisations. Any revision and any reproduction in a digital form requires approval by the Concussion in Sport Group. It should not be altered in any way, rebranded or sold for commercial gain.

ANY ATHLETE WITH A SUSPECTED CONCUSSION SHOULD BE IMMEDIATELY REMOVED FROM PRACTICE OR PLAY AND SHOULD NOT RETURN TO ACTIVITY UNTIL ASSESSED MEDICALLY, EVEN IF THE SYMPTOMS RESOLVE

© Concussion in Sport Group 2017

Figure 2: The Concussion Recognition Tool 5 (CRT5)

7.3 Protocol deviations

A protocol deviation is an unanticipated or unintentional departure from the expected conduct of an approved study that is not consistent with the current research protocol. A protocol deviation may be an omission, addition or change in any procedure described in the protocol.

In the unlikely event that the organisation/site principal investigator is of the opinion that any aspect of the study protocol creates an immediate hazard to a trial patient, they may implement a deviation from or change to the protocol without prior HREC approval. The implemented deviation or change must be reported in a protocol deviation form. The deviation must be reported via the study website by the organization/site principal investigator and reported to the HREC (if applicable).

8. STATISTICAL CONSIDERATIONS

8.1 Power calculations and sample size

In this cohort of players, we conservatively estimate that 50% will have a diagnosis of concussion (this proportion may be higher as players would be screened by telephone advice and VAFA side-line, thereby increasing our power). In the intervention arm, we are aiming for a minimum clinically significant absolute difference of 15%, i.e., 50% of participants to have a diagnosis of concussion within 7 days compared to 35% in the standard care arm. Using 90% power and 0.05 significance level, we will require 480 players to be randomised. We will aim to recruit 500 players to account for loss to follow-up. In 2021, our pilot study of 60 teams (i.e., ~20% of VAFA), during an abridged season due to COVID-19 (~60% of the total length), we had 61 cases of concussions reported. As such, with full league involvement and a complete season, we estimate there to be 693 cases of concussion per year. Even if all clubs do not participate and some players do not enter the trial, we have a large enough eligible population over 2 years for the sample size to be comfortably achieved.

8.2 Analysis of results

8.2.1 Descriptive statistics and primary outcome

Patient characteristics will be presented in a table with descriptive statistics used to present the general characteristics of this cohort. Baseline characteristics will be summarised using means (with standard deviation) if continuous and normal or near-normally distributed, medians (with inter-quartile range) if skewed or ordinal and count (with proportions) if categorical. Differences between means will be assessed using Student's t-test, differences between medians will be assessed using the Wilcoxon rank sum test and differences between categorical variables assessed using the Chi-square test. The primary outcome – the proportion of concussion diagnosis in the two arms - will be computed using the Chi-square test and summarised using Odds Ratio (OR) and reported with 95% confidence intervals (95% CI). Potential variables associated with the primary outcome will be evaluated using ORs and presented with 95%CIs. Hosmer-Lemeshow purposeful variable selection approach will be used to select potential confounding factors identified in univariate analysis ($p<0.25$) into a generalised linear model with the most appropriate distribution family and link function[32]. Akaike information criterion and Bayesian Information Criterion will be used to fit the final model to determine independent predictors of concussion diagnosis. We will report results of the study after the first season (i.e. September 2023).

8.2.2 Secondary outcomes

We will use mixed effects linear models, in accordance with previous research,[33,34] to assess whether the symptom severity scores changed between visits. A modified mixed effects Poisson models with random intercepts for participants will be used to estimate the relative risks (RR) for each binary outcome with 95%CI.[35] These models accounted for positive correlation in the repeated outcomes from the same participant and use the information sandwich estimator to obtain variance estimates. These estimates are considered robust to the error misspecification, take account of any heteroskedasticity and have been found to be preferable for unbiased estimates of risk ratios.[36] Mixed effects regression has been shown to produce robust findings even when imbalance in the data (e.g. loss to follow-up) is present, supporting the use of this model for this study. Time will be treated as a categorical variable (7 days and 14 days) in the models and potentially confounding variables where a demonstrated association ($p < 0.1$) is found with the exposure variable will be included in the models. Postestimation average proportions of the

presence/absence of concussion over the two time points will be generated using the delta-method to calculate the standard errors of predictions and 95%CIs and graphed.[34]

8.2.3 Telehealth

We will report on the challenges and the length of the telehealth consults in a descriptive narrative way.

On day 30, we will assess the usability of the telehealth program using the Telehealth Usability Questionnaire as modified by Shore et al.[37]

Interface Quality				
1	The way I interact with this system is pleasant			Y
2	I like using the system			Y
3	The system is simple and easy to understand	S		Y
4	This system is able to do everything I would want it to be able to do	S		Y
Interaction Quality				
1	I could easily talk to the clinician using the telehealth system		Y	
2	I could hear the clinician clearly using the telehealth system		Y	
3	I felt I was able to express myself effectively		Y	
4	Using the telehealth system, I could see the clinician as well as if we met in person		Y	
Reliability				
1	I think the visits provided over the telehealth system are the same as in-person visits		Y	
2	Whenever I made a mistake using the system, I could recover easily and quickly	S		Y
3	The system gave error messages that clearly told me how to fix problems			Y
Satisfaction and Future Use				
1	I feel comfortable communicating with the clinician using the telehealth system		Y	Y
2	Telehealth is an acceptable way to receive healthcare services	S	Y	Y
3	I would use telehealth services again		Y	
4	Overall, I am satisfied with this telehealth system		Y	Y

Note. Y = taken from the questionnaire with no or slight change; S = Similar item with different wording exists in the questionnaire.

Figure 3: Modified Telehealth Usability Questionnaire

8.2.4 Satisfaction

On day 30 we will assess the participant satisfaction using the Client Satisfaction Questionnaire-8 (CSQ-8).[37,38]

CSQ1	How would you rate the quality of service received?
CSQ2	Did you get the kind of service you wanted?
CSQ3	To what extent has our programme met your needs?
CSQ4	If a friend were in need of similar help, would you recommend our programme to him or her?
CSQ5	How satisfied are you with the amount of help you have received?
CSQ6	Have the services you received helped you to deal more effectively with your problems?
CSQ7	In an overall, general sense, how satisfied are you with the service you have received?
CSQ8	If you were to seek help again, would you come back to our programme?

8.2.5 Intention-to-treat analysis

All analyses will be undertaken on an intention-to-treat basis. It is unlikely that there will be crossover between the two arms.

8.2.6 Missing data

Missingness of data will be examined using Little's chi-square test. If data are missing completely at random, complete case analysis will be used. If data are missing at random, i.e., missingness is not completely random but can be fully accounted for by other variables, the associated variables will be included in all analyses. If data are missing not at random, i.e., missingness is systematically related to the unobserved data, sensitivity analyses will be performed to see how sensitive the results are under different scenarios.

8.2.7 Statistics

A p-value of <0.05 will be deemed as statistically significant. We will use Stata version 17 (Statacorp, College Station, TX) for all analyses.

8.3 Adverse events

Adverse events (AEs) are defined as any untoward medical occurrence in a patient or clinical investigation subject administered an investigational intervention and which does not necessarily have to have a causal relationship with this treatment (adapted from the Note for Guidance on Clinical Safety Data Management: Definitions and Standards for Expedited Reporting (CPMP/ICH/377/95 July 2000).[39]

It is recognised that the patient population of potentially concussed patients may all have adverse experiences and a number of symptoms due to their injury. These will not necessarily constitute an adverse event unless they require significant intervention or are considered to be of concern according to the organisation/site principal investigator's clinical judgement. Adverse events in this study may include (but are not limited to) seizures, head and neck injuries and brain bleeding.

8.4 Serious adverse events

Serious Adverse Events (SAE) are defined in accordance with the Note for Guidance on Clinical Safety Data Management: Definitions and Standards for Expedited Reporting (CPMP/ICH/377/95) (July 2000)[39] as any untoward medical occurrence that:

- Results in death
- Is life-threatening
- Requires inpatient hospitalisation or prolongation of existing hospitalisation
- Results in persistent or significant disability/incapacity
- Is a congenital anomaly/birth defect
- Is an important medical event that may require intervention to prevent one of the previously listed outcomes

A suspected unexpected serious adverse reaction (SUSAR) is an SAE that is not expected based on information that is currently available. Given the intervention of this trial, we do not anticipate many, if any, SUSARs.

8.5 Reporting

SAEs and SUSARs should be reported within 24 hours of identification by telephone or email to the local principal investigator and the coordinating centre. However, consistent

with the advice of Cook et al.,[40] adverse events already defined and reported as study outcomes will not be labelled and reported a second time as SAEs.

Any other reporting requirements mandated by the HREC, and relevant national and local authorities must also be followed. SAEs and SUSARs will be reported to Alfred Hospital Ethics Committee.

For SAEs and SUSARs, a preliminary telephone or e-mail report should be followed by a full report which includes copies of relevant hospital case records and other documents where applicable.

9. FUNDING

9.1 MRFF funding

The INFORMED study is funded by the Medical Research Future Fund (MRFF) MRFF 2021 Traumatic Brain Injury Grant Opportunity (APP 2016112).

9.2 Study budget

Item	**Total cost across the 3-year study period**
Study co-ordinator (Aim 1; VIC)	$152,886
Neuropsychologist (Aim 1; VIC)	$122,309
Clinician (Aim 1; VIC and QLD)	$122,309
CSQ-8	$300

10. RESEARCH TIMELINES

Time frame indicators	Milestones
Aug 2022	Study organisation commenced
Jan 2023	Protocol finalised
Feb 2023	Alfred HREC submission
Mar 2023	Start-up meeting
Mar 2023	Training of critical care triage nurse and neuropsychologist / physiotherapist commences
April 2023	Marketing and distribution of the new phone triage service to VAFA
April 2023	Site activation at The Alfred and study recruitment commences
Nov 2023	50% recruitment completed
Nov 2024	100% recruitment completed
Dec 2024	Query resolution and data cleaning completed
Jan 2025	Database lock
February 2025	Primary analysis completed
Mar 2025	Submission of initial manuscript

11. COVID-19 IMPACT

This project will follow all isolation requirements as dictated by the department of health and Alfred Health clinical practice guidelines. We do not anticipate any additional risk to patients of health care workers from participation in this research project.

12. References

1. Marshall S, Bayley M, McCullagh S, Berrigan L, Fischer L, Ouchterlony D, et al. Guideline for concussion/mild traumatic brain injury and prolonged symptoms: (for Adults 18+ years of age). Ont Neurotrauma Found. 2018;

2. McCrory P, Meeuwisse W, Dvorak J, Aubry M, Bailes J, Broglio S, et al. Consensus statement on concussion in sport—the 5th international conference on concussion in sport held in Berlin, October 2016. Br J Sports Med [Internet]. 2017 Jun 1 [cited 2023 Jan 11];51(11):838–47. Available from: https://bjsm.bmj.com/content/51/11/838

3. Langer L, Levy C, Bayley M. Increasing Incidence of Concussion: True Epidemic or Better Recognition? J Head Trauma Rehabil [Internet]. 2020 Feb [cited 2023 Jan 4];35(1):E60. Available from: https://journals.lww.com/headtraumarehab/Abstract/2020/01000/Increasing_Incidence_of_Concussion__True_Epidemic.16.aspx

4. AFL. The management of concussion in Australian Football. Melbourne, Victoria; 2021.

5. Kara S, Crosswell H, Forch K, Cavadino A, McGeown J, Fulcher M. Less Than Half of Patients Recover Within 2 Weeks of Injury After a Sports-Related Mild Traumatic Brain Injury: A 2-Year Prospective Study. Clin J Sport Med Off J Can Acad Sport Med. 2020 Mar;30(2):96–101.

6. Whitnall L, McMillan TM, Murray GD, Teasdale GM. Disability in young people and adults after head injury: 5–7 year follow up of a prospective cohort study. J Neurol Neurosurg Psychiatry [Internet]. 2006 May 1 [cited 2023 Jan 4];77(5):640–5. Available from: https://jnnp.bmj.com/content/77/5/640

7. Thornhill S, Teasdale GM, Murray GD, McEwen J, Roy CW, Penny KI. Disability in young people and adults one year after head injury: prospective cohort study. BMJ [Internet]. 2000 Jun 17 [cited 2023 Jan 4];320(7250):1631–5. Available from: https://www.bmj.com/content/320/7250/1631

8. McMillan TM, Teasdale GM, Stewart E. Disability in young people and adults after head injury: 12–14 year follow-up of a prospective cohort. J Neurol Neurosurg Psychiatry [Internet]. 2012 Nov 1 [cited 2023 Jan 4];83(11):1086–91. Available from: https://jnnp.bmj.com/content/83/11/1086

9. Maas AIR, Menon DK, Adelson PD, Andelic N, Bell MJ, Belli A, et al. Traumatic brain injury: integrated approaches to improve prevention, clinical care, and research. Lancet Neurol [Internet]. 2017 Dec 1 [cited 2023 Feb 20];16(12):987–1048. Available from: https://www.thelancet.com/journals/laneur/article/PIIS1474-4422(17)30371-X/fulltext

10. Te Ao B, Brown P, Tobias M, Ameratunga S, Barker-Collo S, Theadom A, et al. Cost of traumatic brain injury in New Zealand: evidence from a population-based study. Neurology. 2014 Oct 28;83(18):1645–52.

11. King DA, Hume PA, Hind K, Clark TN, Hardaker N. The Incidence, Cost, and Burden of Concussion in Women's Rugby League and Rugby Union: A Systematic Review and Pooled Analysis. Sports Med [Internet]. 2022 Aug 1 [cited 2023 Jan 17];52(8):1751–64. Available from: https://doi.org/10.1007/s40279-022-01645-8

12. Cantarero G, Choynowski J, St. Pierre M, Anaya M, Statton M, Stokes W, et al. Repeated Concussions Impair Behavioral and Neurophysiological Changes in the Motor Learning System. Neurorehabil Neural Repair [Internet]. 2020 Sep 1 [cited 2023 Jan 10];34(9):804–13. Available from: https://doi.org/10.1177/1545968320943578

13. Asken BM, McCrea MA, Clugston JR, Snyder AR, Houck ZM, Bauer RM. "Playing Through It": Delayed Reporting and Removal From Athletic Activity After Concussion Predicts Prolonged Recovery. J Athl Train [Internet]. 2016 Apr 1 [cited 2023 Jan 11];51(4):329–35. Available from: https://doi.org/10.4085/1062-6050-51.5.02

14. Echemendia RJ, Meeuwisse W, McCrory P, Davis GA, Putukian M, Leddy J, et al. The Concussion Recognition Tool 5th Edition (CRT5): Background and rationale. Br J Sports Med. 2017 Jun;51(11):870–1.

15. Delaney JS, Lamfookon C, Bloom GA, Al-Kashmiri A, Correa JA. Why university athletes choose not to reveal their concussion symptoms during a practice or game. Clin J Sport Med Off J Can Acad Sport Med. 2015 Mar;25(2):113–25.

16. Pietro VD, O'Halloran P, Watson CN, Begum G, Acharjee A, Yakoub KM, et al. Unique diagnostic signatures of concussion in the saliva of male athletes: the Study of Concussion in Rugby Union through MicroRNAs (SCRUM). Br J Sports Med [Internet]. 2021 Dec 1 [cited 2023 Jan 11];55(24):1395–404. Available from: https://bjsm.bmj.com/content/55/24/1395

17. McCrea M, Broglio SP, McAllister TW, Gill J, Giza CC, Huber DL, et al. Association of Blood Biomarkers With Acute Sport-Related Concussion in Collegiate Athletes: Findings From the NCAA and Department of Defense CARE Consortium. JAMA Netw Open [Internet]. 2020 Jan 24 [cited 2023 Jan 11];3(1):e1919771. Available from: https://doi.org/10.1001/jamanetworkopen.2019.19771

18. Jacob D, Unnsteinsdóttir Kristensen IS, Aubonnet R, Recenti M, Donisi L, Ricciardi C, et al. Towards defining biomarkers to evaluate concussions using virtual reality and a moving platform (BioVRSea). Sci Rep [Internet]. 2022 May 30 [cited 2023 Jan 11];12(1):8996. Available from: https://www.nature.com/articles/s41598-022-12822-0

19. Gourley MM, Valovich MTC, Bay RC. Awareness and Recognition of Concussion by Youth Athletes and Their Parents. Athl Train Sports Health Care [Internet]. 2010 Sep [cited 2023 Jan 10];2(5):208–18. Available from: https://journals.healio.com/doi/full/10.3928/19425864-20100524-03

20. Shafqat S, Kvedar JC, Guanci MM, Chang Y, Schwamm LH. Role for Telemedicine in Acute Stroke. Stroke [Internet]. 1999 Oct [cited 2023 Jan 11];30(10):2141–5. Available from: https://www.ahajournals.org/doi/full/10.1161/01.STR.30.10.2141

21. Terkelsen CJ, Nørgaard BL, Lassen JF, Gerdes JC, Ankersen JP, Rømer F, et al. Telemedicine used for remote prehospital diagnosing in patients suspected of acute myocardial infarction. J Intern Med [Internet]. 2002 [cited 2023 Jan 11];252(5):412–20. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1046/j.1365-2796.2002.01051.x

22. du Toit M, Malau-Aduli B, Vangaveti V, Sabesan S, Ray RA. Use of telehealth in the management of non-critical emergencies in rural or remote emergency departments: A systematic review. J Telemed Telecare [Internet]. 2019 Jan 1 [cited 2023 Jan 11];25(1):3–16. Available from: https://doi.org/10.1177/1357633X17734239

23. Moffatt JJ, Eley DS. The reported benefits of telehealth for rural Australians. Aust Health Rev Publ Aust Hosp Assoc. 2010 Aug;34(3):276–81.

24. Meyer BC, Raman R, Hemmen T, Obler R, Zivin JA, Rao R, et al. Efficacy of site-independent telemedicine in the STRokE DOC trial: a randomised, blinded, prospective study. Lancet Neurol [Internet]. 2008 Sep 1 [cited 2023 Jan 11];7(9):787–95. Available from: https://www.sciencedirect.com/science/article/pii/S1474442208701716

25. Gagnon MP, Duplantie J, Fortin JP, Landry R. Implementing telehealth to support medical practice in rural/remote regions: what are the conditions for success? Implement Sci [Internet]. 2006 Aug 24 [cited 2023 Jan 11];1(1):18. Available from: https://doi.org/10.1186/1748-5908-1-18

26. Watanabe M, Jennett P, Watson M. The effect of information technology on the physician workforce and health care in isolated communities: The Canadian picture. J Telemed Telecare [Internet]. 1999 May 1 [cited 2023 Jan 11];5(2_suppl):11–9. Available from: https://doi.org/10.1258/1357633991933477

27. Naidoo N. Asking the answerable question. In: Olaussen A, Bowles KA, Lord B, Williams B, editors. Introducing, Designing and Conducting Research for Paramedics. 1st ed. Melbourne, Australia: Elsevier; 2022.

28. Reade MC, Bass F, Howe B, Seppelt I, Shehabi Y. Considerations for co-enrolment in randomised controlled effectiveness trials in critical care: the SPICE-8 co-enrolment guidelines. Crit Care Resusc J Australas Acad Crit Care Med. 2017 Jun;19(2):110–4.

29. VVED. Victorian Virtual Emergency Department (VVED) [Internet]. Victorian Virtual Emergency Department. 2023 [cited 2023 Jan 17]. Available from: https://www.vved.org.au/

30. Mckay A. ANZCTR - Registration - ACTRN12622000702718 - iRECOveR: Interdisciplinary Rehabilitation for Concussion Recovery [Internet]. 2022 [cited 2023 Jan 17]. Available from: https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=384026&isReview=true

31. NHMRC. National Statement on Ethical Conduct in Human Research (2007) - Updated 2018 | NHMRC [Internet]. 2018 [cited 2023 Jan 16]. Available from:

https://www.nhmrc.gov.au/about-us/publications/national-statement-ethical-conduct-human-research-2007-updated-2018

32. Hosmer Jr DW, Lemeshow S, Sturdivant RX. Applied logistic regression. Vol. 398. John Wiley & Sons; 2013.

33. Leddy J, Hinds AL, Miecznikowski J, Darling S, Matuszak J, Baker JG, et al. Safety and Prognostic Utility of Provocative Exercise Testing in Acutely Concussed Adolescents: A Randomized Trial. Clin J Sport Med Off J Can Acad Sport Med [Internet]. 2018 Jan [cited 2023 Jan 17];28(1):13–20. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5739074/

34. Mitra B, Beck B, Dipnall JF, Ponsford J, Gabbe B, Cameron PA. Long-term outcomes of major trauma patients with concussion. Injury [Internet]. 2023 Jan 1 [cited 2023 Jan 17];54(1):75–81. Available from: https://www.sciencedirect.com/science/article/pii/S0020138322005253

35. Zou G. A Modified Poisson Regression Approach to Prospective Studies with Binary Data. Am J Epidemiol [Internet]. 2004 Apr 1 [cited 2023 Jan 17];159(7):702–6. Available from: https://doi.org/10.1093/aje/kwh090

36. Chen W, Qian L, Shi J, Franklin M. Comparing performance between log-binomial and robust Poisson regression models for estimating risk ratios under model misspecification. BMC Med Res Methodol [Internet]. 2018 Jun 22 [cited 2023 Jan 17];18(1):63. Available from: https://doi.org/10.1186/s12874-018-0519-5

37. Shore J, Hutchison MG, Nalder E, Reed N, Hunt A. Tele-Active Rehabilitation for adolescents with concussion: a feasibility study. BMJ Open Sport Exerc Med [Internet]. 2022 Feb 1 [cited 2023 Jan 17];8(1):e001277. Available from: https://bmjopensem.bmj.com/content/8/1/e001277

38. Attkisson CC, Zwick R. The client satisfaction questionnaire. Psychometric properties and correlations with service utilization and psychotherapy outcome. Eval Program Plann. 1982;5(3):233–7.

39. TGA. Note for guidance on clinical safety data management: definitions and standards for expedited reporting [Internet]. 2000. Available from: https://www.tga.gov.au/resources/publication/publications/note-guidance-clinical-safety-data-management-definitions-and-standards-expedited-reporting

40. Cook D, Lauzier F, Rocha MG, Sayles MJ, Finfer S. Serious adverse events in academic critical care research. CMAJ Can Med Assoc J J Assoc Medicale Can. 2008 Apr 22;178(9):1181–4.